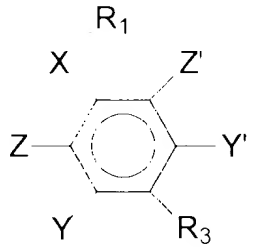


wherein

X is selected from the group consisting of C=O, S=O, C=S, (C=O)-NH, (C=O)-O and (C=O)-S:

R_1 is selected from the group consisting of:

(i) hydrogen, hydroxyl or a hydrocarbon chain from 1 to about 10 carbons long selected from the group consisting of saturated, unsaturated and fluorinated, wherein said hydrocarbon chain is unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, CO_2R^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

(ii) an oligopeptide or peptidomimetic molecule of 1 to 5 amino acids;

(iii) C_3-C_6 cycloalkyl, C_6-C_{10} bicycloalkyl, C_3-C_7 cycloalkylmethyl, or C_7-C_{10} arylalkyl, which may be additionally substituted with R^{11} as defined above;

R_3 is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain or O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, carboxyl and NHR^{11}, wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamid, carbamyl, carbamyloxy or halogen;

(ii) hydrogen; and

(iii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl, or C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

alternatively Z' and R_1 collectively form a ring system selected from the group consisting of:

(a) C_5-C_8 carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R^{11} as defined above; and

(b) C_5-C_{10} heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, carbamide, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone;

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above;

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids; and

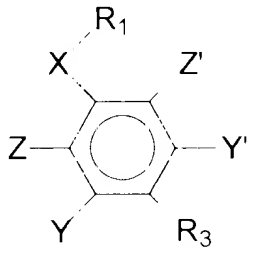
(v) Y' may additionally be hydroxyl;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen;

to effectively inhibit picornaviral replication.

12. (Twice Amended) A method according to claim 8, wherein the picornavirus species is a rhinovirus.

13. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C=O;

R_1 is $-CF_3$;

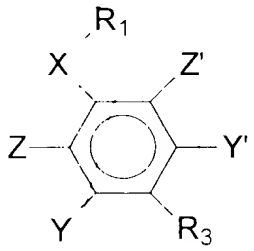
Z and Z′ are hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

R_3 is hydrogen; and

Y and Y′ are selected from the group consisting of –Cl, –I, –Br, $-CF_3$, –F, –CN, –COOH, $-SO_3H$, $-SO_2NH_2$ and -$CONH_2$

to effectively inhibit picornaviral replication.

14. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C= O;

R_1 is $-CF_3$;

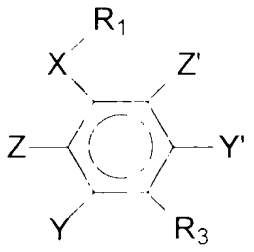
Z is hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

Z′ and R_3 are hydrogen; and

Y and Y′ are selected from the group consisting of –Cl, –I, –Br, $-CF_3$, –F, –CN, -COOH, $-SO_3H$, $-SO_2NH_2$ and -$CONH_2$

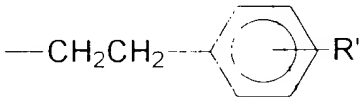
to effectively inhibit picornaviral replication.

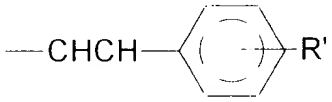
15. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:

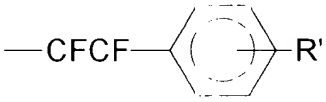


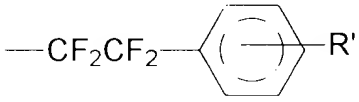
wherein X is –C=O;

R_1 is H, $-CH_3$, $-CF_3$, $CH_3-CH_2-CH_2-CH_2-CH_2-$, CH_3-CH_2-, $CH_3-CH_2-CH_2-$, $CF_3-CF_2-CF_2-CF_2-CF_2-$, –NH–R′′or one of the following phenyl groups









wherein R′ is –OH, $-NH_2$, –COOH, or $-COCH_3$ and R′′ is –OH, $-NH_2$, $-OCH_3$ or $-OCH_2CH_3$;

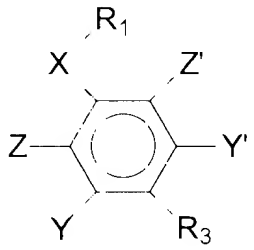
Z and Z′ are hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

R_3 is hydrogen; and

Y and Y′ are $-CF_3$

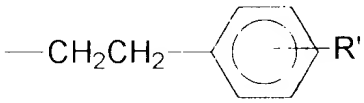
to effectively inhibit picornaviral replication.

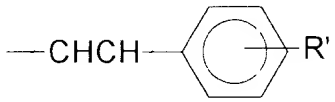
16. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:

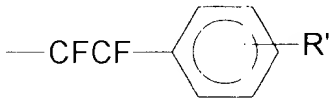


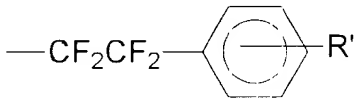
wherein X is –C=O;

R_1 is H, $-CH_3$, $-CF_3$, $CH_3-CH_2-CH_2-CH_2-CH_2-$, CH_3-CH_2-, $CH_3-CH_2-CH_2-$, $CF_3-CF_2-CF_2-CF_2-CF_2-$, –NH–R′′, or one of the following phenyl groups









wherein R′ is –OH, $-NH_2$, –COOH, or $-COCH_3$ and R′′ is –OH, $-NH_2$, $-OCH_3$ and $-OCH_2CH_3$;

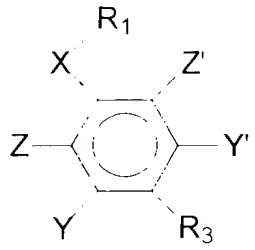
Z is hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

Z′ and R_3 are hydrogen, and

Y and Y′ are $-CF_3$

to effectively inhibit picornaviral replication.

17. (Twice Amended) A method of inhibiting picornaviral replication in a subject, wherein said method comprises the use of a compound with the formula:



wherein X is selected from the group consisting of –C=O-, -S=O-, and -C=S-,

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl, and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain and O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide or a peptidomimetic molecule of 1 to 3 amino acids, joined to the backbone by an oxygen;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, carboxyl, and NHR^{11}, wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;

(ii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl and C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, carbamide, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone;

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above;

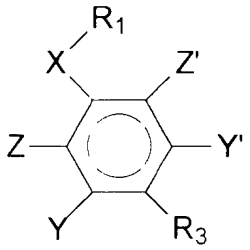
(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids; and

(v) Y' may additionally be hydroxyl;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen

to effectively inhibit picornaviral replication.

19. (Once Amended) A method of inhibiting picornaviral replication in a subject, wherein said method comprises the use of a compound with the formula:



wherein X is selected from the group consisting of –C=O-, -S=O-, and -C=S-;

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl, and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain and O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids[, an oligopeptide of 1 to 3 amino acids] joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, carboxyl, and NHR^{11}, wherein R^{11} is defined as above;

Z′ is selected from the group consisting of:

(i) hydroxyl, amino, carbamide, carbamyl, carbamyloxy, and halogen;

(ii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl and C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y′ are independently selected from the group consisting of:

(i) hydrogen, halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, carbamide, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone;

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above;

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids, and

(v) Y' may additionally be hydroxyl;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen;

to effectively inhibit picornaviral replication.